What are the Effects of Ultrafine Particles?

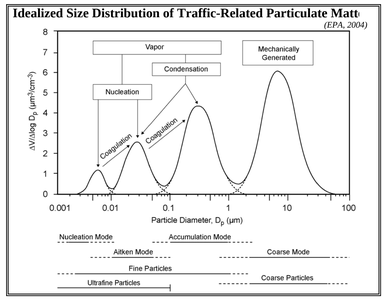
Presenter: Günter Oberdörster

University of Rochester PM Center

research and development

Background

- The EPA currently regulates PM on the basis of mass in two size ranges: less than 2.5μ and 2.5 – 10μ. However, several recent studies suggest that very small, so called ultrafine particles (less than 0.1μ), may be linked with adverse health effects. These particles have very little mass and so are not likely addressed by the current PM standards.
- The figure below depicts the 4 modes of ambient PM. Although the mass of ultrafine particles (UFP) is very low (background levels between 0.5 – 2 μg/m³), it can increase several fold during high pollution episodes or on highways to very high number concentrations (up to 10 million UFP/cm³).
- UFP have a very high specific surface area (see table below) which in general makes them potentially more reactive chemically and biologically compared to larger-sized particles. The larger surface area can function as a carrier for gaseous and semi-volatile co-pollutants.
- The chemical composition of ambient UFP includes elemental and organic carbon compounds, heavy metals and inorganic compounds, with the smaller UFP (<~20 nm) having higher amounts of organics.
- Because of their small size, UFP biokinetics are quite different from larger-sized particles with respect to endocytosis and transcytosis; furthermore, they can distribute to target sites outside the respiratory tract, including the cardiovascular system and the CNS.
- Based on these distinctly different attributes, the hypothesis was proposed that ambient UFP can induce significant health effects.

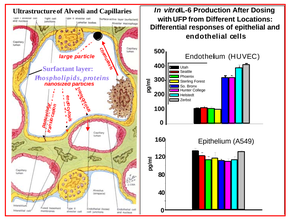


Particle Number and Particle Surface Area Per 10 μg/m³ Airborne Particles		
Diameter μm	Number cm⁻³	Surface Area μm²/cm³
5	153,000,000	12,000
20	2,400,000	3,016
250	1,200	240
5,000	0.15	12

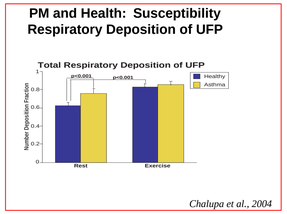
Science Questions

- Do results from epidemiology support the UFP hypothesis?
- Are deposition and disposition of inhaled UFP different from fine and coarse particles?
- Do inhaled UFP reach extrapulmonary remote target organs?
- What is the evidence that inhaled UF can cause direct effects in remote organs?
- Which subpopulations are most likely to be susceptible to UFP?

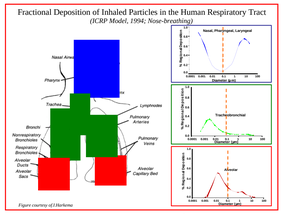
UFP cross the alveolo-capillary barrier



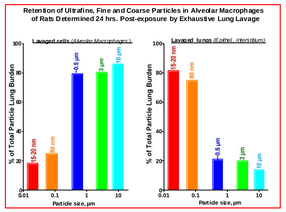
High UFP deposition is further increased in asthmatics



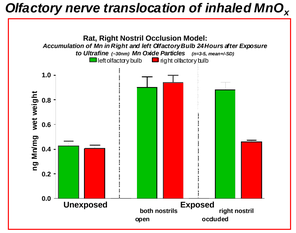
UFP deposition is high in all regions of resp. tract



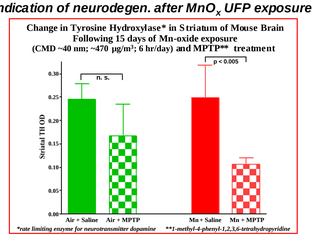
UFP "escape" alveolar macrophage phagocytosis



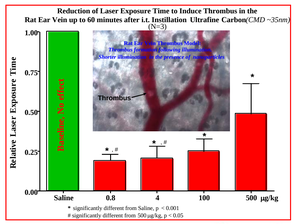
Olfactory nerve translocation of inhaled MnO_x



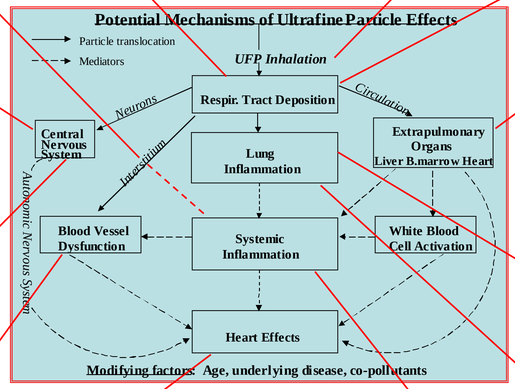
Indication of neurodegen. after MnO_x UFP exposure



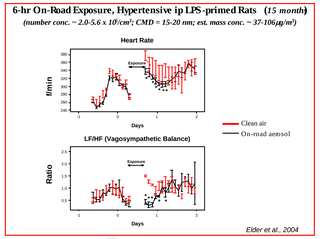
Accelerated thrombus formation after UFP expos.



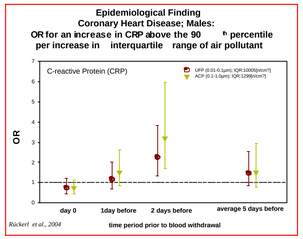
Potential Mechanisms of Ultrafine Particle Effects



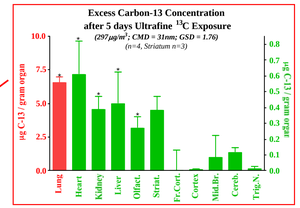
Heart rate and HRV changes in rats following on-road exposure (CMD = 29 nm)



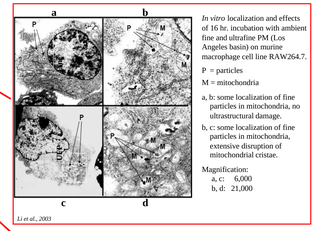
Epidemiological evidence of systemic inflammation associated with exposure to UFP



Translocation of inhaled UFP to extrapulm. organs



Mitochondrial localization of UFP and damage



In vitro localization and effects of 16 hr. incubation with ambient fine and ultrafine PM (Los Angeles basin) on murine macrophage cell line RAW264.7.

P = particles

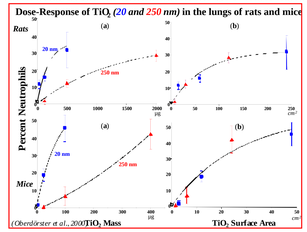
M = mitochondria

a, b: some localization of fine particles in mitochondria, no ultrastructural damage.

b, c: some localization of fine particles in mitochondria, extensive disruption of mitochondrial cristae.

Magnification:
a, c: 6,000
b, d: 21,000

Surf. area is better dosemetric for UFP than mass



Conclusions

- These data show significant effects of UFP in epidemiological, controlled clinical and toxicological *in vivo* and *in vitro* studies.
- Because of their small size, the fate of inhaled UFP following deposition in the respiratory tract differs from fine and coarse particles.

  Endocytosis, transcytosis, subcellular distribution and translocation of UFP across epithelium and along neuronal axons to extra-pulmonary organs have been demonstrated.
- Thus, depending on chemical composition and dose, UFP are likely to induce not only direct effects (oxidative stress; inflammation) in the respiratory tract, cardiovascular system and CNS but also indirect systemic effects *via* released mediators.
- UFP exposure could predispose or accelerate heart attacks, arrhythmias, and strokes in individuals with compromised cardio-vascular systems (*e.g.,* diabetics) *via* endothelial dysfunction and altered clotting.

Future Directions

- Determine potential of inhaled UFP to cause direct effects on non-pulmonary organs (e.g. CNS, heart)
- Evaluate and quantify translocation pathways to other organs for UFP of different chemical composition
- Identify mechanisms of direct and indirect thrombogenic effects of UFP: platelet and endothelial cell activation; oxidative stress responses
- Perform repeated exposures to ambient UFP in animal models of human compromised state
- Design controlled clinical and epidemiological cohort studies focusing on susceptible populations

Impact

- Since the current mass-based standards do not protect against the effects of ultrafine particles, these data will provide important information to the OAR as it considers whether a standard based on particle number or surface area would be appropriate.
- Monitoring of UFP in several major cities should begin so that time-series epidemiological studies can be completed in time for the next NAAQS review.

Health and Exposure